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A systematic review of evidence-based interventions for child and adolescent mental health problems in low- and middle-income countries

Wagner Silva Ribeiro [a,*], Antônio José Grande [b], Mauricio Scopel Hoffmann [c], Carolina Ziebold [d], David McDaid [a], Andra Fry [e], Clayton Peixoto [b], Cláudio Miranda [f], Derek King [a], Cristiane Damiani Tomasi [g], Christine Faustino [b], Sandra Leone [h], Silvia Moraes [i], Antonio Augusto Schäfer [g], Veronica Alves [f], Maria Ines Rosa [g], Sara Evans-Lacko [a]

[a] Care Policy and Evaluation Centre, London School of Economics and Political Science, London, United Kingdom
[b] Universidade Estadual de Mato Grosso do Sul, Campo Grande, Brazil
[c] Universidade Federal de Santa Maria, Santa Maria, Brazil
[d] Departamento de Psiquiatria, Universidade Federal de São Paulo, São Paulo, Brazil
[e] Library, London School of Economics and Political Science, London, United Kingdom
[f] Universidade Federal de Alagoas, Maceió, Brazil
[g] Universidade do Extremo Sul de Santa Catarina, Criciúma, Brazil
[h] Universidade Federal de Mato Grosso do Sul, Campo Grande, Brazil
[i] FIOCRUZ Mato Grosso do Sul, Campo Grande, Brazil

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ABSTRACT

Background: Treatments for mental health problems in childhood and adolescence have advanced in the last 15 years. Despite advances in research, most of the evidence on effective interventions comes from high-income countries, while evidence is scarce in low- and middle-income countries (LMICs), where 90% of world's children and adolescents live. The aim of this review was to identify evidence-based interventions tested in LMICs to treat or prevent child and adolescent mental health problems.

Methods: We conducted a systematic review of seven major electronic databases, from January 2007 to July 2019. We included randomised or non-randomised clinical trials that evaluated interventions for children or adolescents aged 6 to 18 years living in LMICs and who had, or were at risk of developing, one or more mental health problems. Results were grouped according to the studied conditions. Due to the heterogeneity of conditions, interventions and outcomes, we performed a narrative synthesis. The review was registered at PROSPERO under the number CRD42019129376.

Findings: Of 127,466 references found through our search strategy, 107 studies were included in narrative synthesis after the eligibility verification processes. Nineteen different conditions and nine types of interventions were addressed by studies included in the review. Over 1/3 of studied interventions were superior to comparators, with psychoeducation and psychotherapy having the highest proportion of positive results. One-third of studies were classified as presenting low risk of bias.

Interpretation: This review shows that different interventions have been effective in LMICs and have the potential to close the mental health care gap among children and adolescents in low-resource settings.

1. Introduction

Child and adolescent mental health problems represent a significant burden worldwide [1]. Mental disorders are experienced by 10 to 20% of children and adolescents globally [2]. More than one-third of all mental disorders begin before the age of 14 years, and nearly one-half by

Abbreviations: LMICs, low- and middle-income countries; HICs, high-income countries; EMBASE, Excerpta Medica dataBASE; CINAHL, Cumulative Index for Nursing and Allied Health Literature; LILACS, Latin American and Caribbean Literature on Health Sciences; BDENF, Banco de dados em Enfermagem; IBECS, Integrated Building Environmental Communications System.

* Corresponding author at: Houghton Street, WC2A 2AE London, United Kingdom.
E-mail address: W.Silva-Ribeiro@lse.ac.uk (W.S. Ribeiro).

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the age of 18 [3].

Child and adolescent mental health problems can persist over the lifespan and are related to impairment in educational, economic, developmental and personality formation [4–6]. They are the leading cause of years lived with disability among young people [7], and are also associated with significant costs. For The State of the World's Children 2021 report [2], it was estimated that the annual societal cost of youth mental health conditions was around US$340.2 billion purchasing power parity adjusted (PPP) dollars. Most of the burden falls on low- and middle-income countries (LMICs). These findings suggest a strong rationale for investing in early prevention and treatment of child and adolescent mental health problems and for supporting the implementation of evidence-based interventions to mitigate these problems and associated consequences.

In recent decades, progress has been made towards the development and evaluation of interventions to treat and prevent child and adolescent mental health problems in high-income countries (HICs), and there is robust evidence of effectiveness of interventions for many of these problems [8–10]. However, research is scarcer in LMICs [11] where almost 90% of world's children and adolescents live, and where young people can comprise up to 50% of the total population [12,13] – a systematic review published in 2013 [8], for example, found 54 studies carried out in LMICs, but concluded that results from these studies were "still tentative", and that the most robust evidence came from HICs.

Due to the lack of evidence from LMICs, many interventions carried out in these countries take, as a reference, evidence produced in HICs. Considering the more limited human and financial resources which can constrain the types of care available and how they are delivered, it is unclear whether interventions tested in HICs can be as effectively implemented in LMICs. Moreover, contextual factors, such as high levels of economic inequality, increased exposure to violence, conflict-related trauma and deprivation, which are more common in LMICs, might impact efficacy, especially of psychotherapy.

The overarching aim of this systematic review was to identify evidence-based interventions evaluated in LMICs for the treatment of child and adolescent mental health problems, and/or their prevention (among high-risk groups). Given the limited financial resources for specialist mental health care in LMICs, we considered a broad range of interventions that could be delivered in a range of settings including schools, primary care, and those which could be delivered in the community by lay people.

2. Methods

We conducted a systematic review of the literature published in scientific journals and grey literature. The study design and report of this review is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14]. The protocol of this review is registered in PROSPERO under the number CRD42019129376 and has been previously published [15].

We included randomised or non-randomised controlled trials, as well as economic evaluations or modelling analysis, which evaluated any types of interventions to treat or prevent any mental health problems or mental disorders among 6–18-year-old children and adolescents living in low- or middle-income countries. Therefore, only studies conducted in countries listed as LMICs in the World Bank Classification [16] were included. For this review, the classification refers to the year 2019. We decided to include school-age children (6 years and older) for the sake of feasibility, both of the review and of potential implementation of interventions in community-based settings.

Notwithstanding non-randomised trials having more potential for biased results, we decided to include such studies because the literature suggests that intervention studies in LMICs might be scarce [8,11]. Considering that randomised trials (RCTs) demand economic and human resources that are not easily available in LMICs, we expected that just a small number of RCTs might be available, which justifies the inclusion of non-randomised trials [17].

We included in our review studies which tested any types of interventions to treat any types of mental health problems among children and adolescents. We did not establish any restrictions in relation to, e.g., intervention configuration (i.e., individual, family, group, remote/online etc.), delivery settings or delivery agent. When available, such information was extracted from studies and considered in our synthesis of evidence.

We also included any types of mental health problems, be them existing metal health disorders with a clinical diagnosis, or any mental health symptoms, including psychological distress. The only requirement for studies to be included was that they should have assessed mental health problems using any validated instrument, including screening tools, scales of symptoms or diagnostic assessment tools.

We considered, as primary outcome, improvement of participants' mental health status, by reducing either mental health symptoms or associated impairment.

No language restrictions were used.

Only studies published from 2007 onwards were included, because this was the year in which child and adolescent mental health became prominent as a global public health challenge [18].

The search was carried out in July 2019 in the following databases: MEDLINE Ovid, EMBASE Ovid, PsycINFO Ovid, CINAHL plus, LILACS (Latin American and Caribbean Health Sciences), BDENF (Brazilian Nursing Database) and IBECS (The Spanish Bibliographic Index of the Health Sciences). Considering that our main aim was to identify any interventions to treat any mental health problems in LMICs, we ran, with the support of a librarian who is an expert in systematic reviews (AF), a very sensitive search which included, as search terms, all potential definitions of mental health problems (from more generic terms, such as "mental health" and "mental disorders", to specific diagnoses, such as "depressive disorder", "anxiety etc.). Search terms also included all potential variations of interventions and, all countries listed in the World Bank Classification as LMICs. Our search strategy, including a detailed list of search terms, is available in Appendix 1.

We did not update the search to included studies published after 2019 because several trials were compromised due to restrictions of the COVID-19 pandemic [19].

We checked reference lists of all included studies and relevant review articles identified through our search for additional references. We emailed experts in the field about other published and unpublished studies that might be eligible for inclusion.

2.1. Data collection and analysis

To ensure reliability between reviewers, we ran a pilot study in which 5% of all references were independently screened by pairs of different reviewers. A committee comprising three mental health research experts (WSR, DM, SEL) resolved between-reviewer divergences. Following identification of reasons for divergence, a subsequent meeting was held with the review team to resolve any systematic errors and clarify any outstanding questions when screening references. References with conflicts were then revised and re-categorised by WSR.

After the screening team was retrained, the remaining 95% of references were equally divided among reviewers and each title and abstract were screened independently. Considering the large number of references retrieved from the databases, a team of 66 reviewers performed the screening of titles and abstracts. This team comprised ten researchers with experience in systematic reviews plus a group of 56 medical students who were trained by two leading members of our team (AJG and WSR) and supervised by two senior researchers (AJG and AAS) as part of a discipline on systematic review and meta-analysis. Based on our inclusion criteria, reviewers classified references into three categories: "no", "yes", and "maybe". References classified as "no" were excluded. Those classified as "yes" or "maybe" were selected for the full text screening phase and were analysed again against inclusion/

Table 1
Trials on interventions to treat child and adolescent mental health problems in low- and middle-income countries.

	Country	Age (years)	Condition	Study type	Dates	Intervention	Participants	Control	Effect
Abadi, 2008	Iran	9–12	ADHD	No-randomised trial	Not reported	Yoga	20	20	Positive
Abbasi, 2011	Iran	7–13	ADHD	RCT- double-blinded	Not reported	Acetyl-L-Carnitine + methylphenidate	20	20	Not significant
Abdollahian, 2013	Iran	7–9	ADHD	Quasi-experimental	Not reported	CBT	15	15	Positive
Amiri, 2008	Iran	6–15	ADHD	RCT- double-blinded	2006–07	Modafinil	30	30	Not significant
Arabgol, 2009	Iran	3–6	ADHD	RCT- no blindness	Not reported	Reboxetine	12	12	Not significant
Assareh, 2017	Iran	6–12	ADHD	RCT- double-blinded	2009–10	Omega 6 + methylphenidate	20	20	Not significant
Cao, 2018	China	6–13	ADHD	RCT- no blindness	2016–17	Repetitive transcranial magnetic stimulation	20	19	Positive
Coelho, 2017	Brazil	7–14	ADHD	No-randomised trial	2011–15	CBT+ methylphenidate	30	30	Not significant
Dashti, 2014	Iran	6–12	ADHD	RCT- double-blinded	2010–11	Omega 3	28	29	Not significant
Davari-Ashtlani, 2010	Iran	6–12	ADHD	RCT- double-blinded	Not reported	Buspirone	18	16	Not significant
Dutta, 2012	India	6–12	ADHD	RCT- double-blinded	Not reported	Memory syrup	56	30	Positive
El Baza, 2016	Egypt	6–16	ADHD	RCT- no blindness	Not reported	Magnesium	9	9	Not significant
Emadian, 2016	Iran	7–12	ADHD	Quasi-experimental	2015	Narrative therapy	10	10	Not significant
						Computerised cognitive rehabilitation	10		Not significant
Garcia Lara, 2014	Mexico	15–21	ADHD	Quasi-experimental	Not reported	Cognitive intervention program	5	15	Not significant
Garg, 2014	India	6–14	ADHD	RCT- no blindness	2010–12	Atomoxetine	25	26	Not significant
Ghajar, 2018	Iran	6–17	ADHD	RCT- double-blinded	2016–17	L-carnosine + methylphenidate	25	25	Not significant
Hariri, 2012	Iran	6–11	ADHD	RCT- double-blinded	Not reported	Omega 3	53	50	Positive
Hashemian, 2015	Iran	7–12	ADHD	RCT- no blindness	Not reported	Bupropion			Not significant
Jafarinia, 2012	Iran	9.4 (mean)	ADHD	RCT- double-blinded	2008–09	Bupropion	20	20	Not significant
Khalil iKermani, 2016	Iran	8–11	ADHD	RCT- no blindness	2013	Working memory training	30	30	Positive
Keshavarzi, 2014	Iran	10.1 (mean)	ADHD	No-randomised trial	Not reported	Sleep training + methylphenidate			mixed
Kiani, 2017	Iran	13–15	ADHD	RCT- double-blinded	Not reported	Mindfulness meditation	15	15	Not significant
Kousha, 2019	Iran	9.3 (mean)	ADHD	Quasi-experimental	2015–16	Positive Parenting Programme + methylphenidate			Not significant
Lan, 2018	China	10.9 (mean)	ADHD	RCT- no blindness	Not reported	Executive function training	27	26	Not significant
						Social skills training	27		Not significant
Looyeh, 2012	Iran	9–11	ADHD	RCT- no blindness	Not reported	Narrative therapy	3	7	Not significant
Meftagh, 2014	Iran	8–10	ADHD	Quasi-experimental	Not reported	Methylphenidate	17	15	Positive
						Behavioural mother training	15		Positive
						Child verbal self-instruction training	15		Positive
Mishra, 2016	India	12 (mean)	ADHD	RCT- double-blinded	Not reported	Online neuroplasticity targeted remediation	11	7	Not significant
Moghaddam, 2017	Iran	9.5 (mean)	ADHD	RCT- double-blinded	2014	PUFA + Methylphenidate	20	20	Not significant
Mohagheghi, 2017	Iran	9.5 (mean)	ADHD	RCT- double-blinded	Not reported	Theta suppression/beta enhancement	28	26	Not significant
Mohammadi, 2010	Iran	9.6 (mean)	ADHD	RCT- double-blinded	Not reported	Agomelatine	19	19	Not significant

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Table 1 (*continued*)

	Country	Age (years)	Condition	Study type	Dates	Intervention	Participants	Control	Effect
Mohammadi, 2012	Iran	9.6 (mean)	ADHD	RCT- double-blinded	Not reported	Melatonin + Methylphenidate	20	20	Not significant
Mohammadi, 2012a	Iran	10.1 (mean)	ADHD	RCT- double-blinded	Not reported	Buspirone	26	24	Negative
Mohammadi, 2014	Iran	6–12	ADHD	RCT- no blindness	2011	Working memory training + methylphenidate	23	25	Positive
Mohammadi, 2015	Iran	9.1 (mean)	ADHD	RCT- double-blinded	2012–13	Memantine	22	18	Not significant
Mohammadzadeh, 2019	Iran	8.2 (mean)	ADHD	RCT- double-blinded	Not reported	Omega 3 + Methylphenidate	33	33	Not significant
Perera, 2012	Sri Lanka	9.4 (mean)	ADHD	RCT- double-blinded	Not reported	Omega 3 + Omega 6	48	46	Positive
Pisacco, 2018	Brazil	13.1 (mean)	ADHD	RCT- no blindness	Not reported	Text production + working memory training	24	23	Positive
Rajender, 2012	India	7–11	ADHD	RCT- no blindness	Not reported	Cognitive retraining techniques	10	10	Positive
Riahi, 2018	Iran	8.5 (mean)	ADHD	RCT- double-blinded	Not reported	Pramipexole + methylphenidate	30	30	Not significant
Salardini, 2016	Iran	10.3 (mean)	ADHD	RCT- no blindness	2014–14	Agomelatine	25	25	Not significant
Yang, 2012	China	9.5 (mean)	ADHD	RCT- single-blinded	Not reported	Methylphenidate (osmotic release oral system)	57	85	Not significant
Yusuf, 2019	Turkey	7–12	ADHD	RCT- no blindness	Not reported	Positive Parenting Programme	23	25	Positive
Ahmadi, 2018	Afghanistan	12–18	PTSD	Quasi-experimental	Not reported	Memory specific training	8	8	Not significant
						Trauma-focused CBT	8		Not significant
Barron, 2013	Palestine	11–14	PTSD	RCT- no blindness	Not reported	CBT-based trauma recovery programme	90	50	Positive
Berger, 2009	Sri Lanka	9–15	PTSD	Quasi-experimental	2006	ERASE Stress Programme	84	82	Positive
Brillantes-Evangelista, 2013	Philippines	13–18	PTSD	Quasi-experimental	Not reported	Visual arts group	11	11	Positive
						Poetry group	11		Positive
Catani, 2009	Sri Lanka	8–14	PTSD	RCT- no blindness	Not reported	Narrative exposure therapy	16	15	Not significant
Chen, 2014	China	14.5 (mean)	PTSD	RCT- no blindness	2010–11	Sort-term CBT	10	12	Not significant
						General support intervention	10		Not significant
Damra, 2014	Jordan	10–12	PTSD	RCT- no blindness	2012	Trauma-focused CBT	9	9	Positive
Dawson, 2018	Indonesia	7–14	PTSD	RCT- double-blinded	2011–12	Trauma-focused CBT	32	32	Not significant
Hasanovic, 2009	Bosnia	12–15	PTSD	No-randomised trial	2005–06	Psychosocial assistance	336	72	Positive
Jaberghaderi, 2019	Iran	8–12	PTSD	RCT- single-blinded	Not reported	CBT	25	53	Positive
						Eye movement disentisation and reprocessing	24		Positive
Jordans, 2010	Nepal	11–14	PTSD	RCT- no blindness	Not reported	CBT + cooperative play + expressive exercises	164	161	Not significant
Kane, 2016	Zambia	5–18	PTSD	RCT- single-blinded	2012–13	Trauma-focused CBT	131	126	Positive
Lang-Nielson, 2012	Palestine	12–17	PTSD	RCT- no blindness	2009–10	Writing for recovery	66	58	Not significant
Layne, 2008	Bosnia	13–19	PTSD	RCT- no blindness	2000–01	Trauma and grief component therapy	66	61	Not significant
O'Callaghan, 2013	Democratic Republic of Congo	12–17	PTSD	RCT- single-blinded	Not reported	Trauma-focused CBT	24	28	Positive
O'Callaghan, 2015	Democratic Republic of Congo	14–17	PTSD	RCT- single-blinded	2011–12	Trauma-focused CBT	26	22	Positive
Qouta, 2012	Palestine	10–13	PTSD	RCT- no blindness	2008–09	Teaching recovery techniques	232	240	Positive
Shein-Szydlo, 2016	Mexico	12–18	PTSD	RCT- no blindness	Not reported	CBT	50	50	Positive

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Table 1 (*continued*)

	Country	Age (years)	Condition	Study type	Dates	Intervention	Participants	Control	Effect
Tol, 2008	Indonesia	7–15	PTSD	RCT- no blindness	2006	CBT + cooperative play + expressive exercises	182	222	Positive
Tol, 2012	Sri Lanka	9–12	PTSD	RCT- no blindness	2007–08	CBT + cooperative play + expressive exercises	76	78	Mixed
Tol, 2014	Burundi	8–17	PTSD	RCT- no blindness	2006–07	CBT + cooperative play + expressive exercises	122	123	Not significant
Afshari, 2014	Iran	9–13	Anxiety	RCT- no blindness	2011–12	CBT	10	10	Not significant
						Emotion-focused CBT	10		Not significant
Ahmadi, 2017	Malaysia	9–11	Anxiety	Quasi-experimental	Not reported	Eclectic therapy	20	21	Positive
						Eclectic therapy + maternal psychoeducation	20		Not significant
Arman, 2017	Iran	12–20	Anxiety	RCT- double-blinded	2011–12	CBT + d-Cyclomerize	18	18	Not significant
Aydin, 2010	Turkey	12–14	Anxiety	RCT- no blindness	Not reported	CBT	19	21	Not significant
Costa, 2013	Brazil	7–17	Anxiety	RCT- double-blinded	Not reported	Clomipramine	9	11	Not significant
						Fluoxetine	10		Not significant
Ebesutani, 2016	Iran	8–11	Anxiety	RCT- no blindness	Not reported	Modular CBT	11	10	Not significant
						CBT hypnotherapy	11		Not significant
Ebrahiminejad, 2016	Iran	14.5 (mean)	Anxiety	Quasi-experimental	2013	Mindfulness-based cognitive therapy	12	13	Positive
Karbasi, 2010	Iran	12–17	Anxiety	RCT- no blindness	2008–09	Semi-attendence CBT + in-person CBT	20	20	Not significant
Salari, 2018	Iran	6–12	Anxiety	RCT- no blindness	Not reported	Parent-directed CBT	15	19	Not significant
Salum, 2018	Brazil	7–11	Anxiety	RCT- double-blinded	2011–12	CBT + attention bias modification	21	20	Positive
Sevi-Tok, 2019	Turkey	8–12	Anxiety	RCT- no blindness	Not reported	CBT	15	15	Not significant
Araya, 2013	Chile	14.5 (mean)	Depression	RCT- no blindness	Not reported	CBT	1219	1289	Positive
Bella-Awusah, 2016	Nigeria	14–17	Depression	RCT- no blindness	Not reported	CBT	20	20	Positive
Bolton, 2007	Uganda	14–17	Depression	RCT- no blindness	2005	Interpersonal psychotherapy	105	104	Positive
						Creative play intervention			Not significant
Gaete, 2016	Chile	15.9 (mean)	Depression	RCT- single-blinded	Not reported	CBT	229	113	Not significant
Hashemian, 2015	Iran	7–11	Depression	RCT- no blindness	Not reported	Neurofeedback + fluoxetine	14	14	Not significant
Neshat-Doost, 2013	Iran	14.9 (mean)	Depression	RCT- no blindness	Not reported	Memory specific training	12	11	Positive
Saw, 2019	Malaysia	16	Depression	RCT- no blindness	Not reported	CBT	10	10	Positive
Singhal, 2018	India	13–18	Depression	RCT- no blindness	2012–13	Coping-skills programme	65	55	Positive
Adibsereshki, 2015	Iran	7–12	ASD	Quasi-experimental	Not reported	Theory of mind training	12	12	Not significant
Eslamzadeh, 2018	Iran	6–17	ASD	RCT- double-blinded	2015–16	Risperidone + Atomoxetine	20	20	Not significant
Fazlioglu, 2008	Turkey	7–12	ASD	No-randomised trial	Not reported	Sensory integration programme	15	15	Not significant
Gattino, 2011	Brazil	7–12	ASD	RCT- no blindness	Not reported	Music therapy	12	12	Positive
Ghasemtabar, 2015	Iran	7–12	ASD	No-randomised trial	Not reported	Music therapy	13	14	Not significant
Alaghband-Rad, 2009	Iran	7–18	OCD	RCT- double-blinded	1999–2002	Citalopram	14	15	Not significant
Shabani, 2019	Iran	12–18	OCD	RCT- single-blinded	Not reported	Acceptance and commitment therapy + SSRI	22	25	Not significant
Jafari, 2011	Iran	6	ODD	Quasi-experimental	2008–09	Play therapy	8	8	Positive

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Table 1 (*continued*)

	Country	Age (years)	Condition	Study type	Dates	Intervention	Participants	Control	Effect
Morshed, 2019	Iran	6–10	ODD	RCT- no blindness	2012	Individual play therapy	15	15	Positive
Baker-Henningham, 2012	Jamaica	3–6	Conduct disorder	RCT- double-blinded	2009–10	Incredible Years Teacher Training	8	8	Not significant
She, 2016	China	16–18	Schizophrenia	RCT- single-blinded	2012–14	Self-consistency group intervention	30	30	Positive
Ghanizadeh, 2016	Iran	6–18	Tic disorder	RCT- no blindness	Not reported	Aripiprazole	16	20	Not significant
Sang, 2018	China	9–12	Internalising behaviour	RCT- no blindness	Not reported	CBT-based social skills training	16	13	Positive
Ojlambo, 2014	Uganda	10–12	Behavioural problems	RCT- no blindness	Not reported	Active play therapy	30	30	Not significant
Raine, 2015	Mauritius	8–16	Behavioural problems	RCT- double-blinded	2009–11	Omega 3	100	100	Positive
Moharreri, 2017	Iran	7–10	Anxiety + depression	RCT- no blindness	Not reported	Behavioural training programme	18	17	Not significant
Garg, 2015	India	6–14	ODD + ADHD	RCT- single-blinded	2010–12	Methylphenidate	15	22	Not significant
Safavi, 2016	Iran	3–6	ODD + ADHD	RCT- no blindness	Not reported	Risperidone + Aripiprazole	20	20	Not significant
Koolaee, 2014	Iran	6–7	Aggressive behaviour	Quasi-experimental	2013	Dance/movement therapy	15	15	Not significant
Nkrumah, 2015	Ghana	9–11	Impulsive behaviour	RCT- no blindness	Not reported	Cognitive modelling	27	27	Positive
Adibsereshki, 2016	Iran	14–18	Intellectual disability	Quasi-experimental	Not reported	Emotional intelligence training	16	16	Positive
Alavi, 2013	Iran	12–18	Previous suicide attempt	RCT- no blindness	2011–12	CBT	15	15	Positive
Barron, 2017	Palestine	10–18	Complicated grief	Quasi-experimental	Not reported	Emotional intelligence training	79	79	Positive
Pretorius, 2010	South Africa	8–11	History of sexual abuse	Quasi-experimental	Not reported	Group therapy	8	8	Not significant

exclusion criteria after full texts had been obtained and read. Considering the high number of references, titles, abstract and full-text articles were single-screened.

The web-based Covidence (www.covidence.org) tool was used for the management and screening of references.

Three pairs of reviewers extracted data independently following literature recommendation [20]. Data were extracted using the extraction form developed by our team and stored in Microsoft Excel spreadsheet.

We sent two emails (one initial, and one reminder) to corresponding authors to request any missing data or incompletely reported study details.

2.2. Data synthesis

Results were grouped according to the studied conditions, which resulted in five categories: (i) attention-deficit and hyperactivity disorders (ADHD), (ii) post-traumatic stress disorder (PTSD), (iii) anxiety, (iv) depression, and (v) other conditions, which comprised conditions which had a small number of studies.

Considering the heterogeneity of conditions, interventions, and outcomes, we did a narrative synthesis [21] based on the primary outcome reported in each study. We classified effects of studies into four categories: 1) positive, when results favoured the intervention; 2) negative, when results favoured the comparator (control group); 3) neutral, when no statistically significant differences were found between intervention and comparator; and 4) mixed, when study reported conflicting results (e.g., positive effect for a subset of symptoms, or a gender, or a type of psychotherapy, and neutral or negative effect for another subset of symptoms, gender or psychotherapy). This classification was based on statistical parameters extracted from the included studies or, in studies which did not provide appropriate parameters, on all information available (e.g., graphs, or narrative reports from authors). In the context of this review, positive results mean that interventions were more effective than comparators in improving the primary outcome, which was defined as reduction of symptoms of target mental health conditions.

Considering the variety of interventions and their variations (e.g., different variations of cognitive-behavioural psychotherapy (CBT) and other psychological interventions, different psychotropic medicines etc.), we grouped interventions into the following nine broad categories: 1) pharmacological interventions, which include all psychotropic medicines; 2) psychotherapy, which included all different types of psychotherapies and their variations (e.g., CBT, eclectic psychotherapy, play therapy etc.); 3) psychoeducation, which included interventions based on the provision of guidance/information about mental health-related subjects (e.g., parenting skills programmes, social skills training etc.); 4) neurocognitive interventions, which included interventions aiming at modifying/strengthening any dimensions of cognitive functioning (e.g., working memory or executive function training); 5) neuromodulation, which included interventions aiming at modifying/strengthening brain activity (e.g., repetitive transcranial magnetic stimulation); 6) meditation, which included yoga and mindfulness meditation; 7) dietary supplementation, which included prescription of any micro- or macronutrients (e.g., Omega 3, L-carnosine etc.); 8) physical activity (e.g., dance or other types of physical exercises); and 9) combined interventions, which included the combination of at least two of the former different types of interventions (e.g., CBT (psychotherapy) combined with attention bias modification (neurocognitive), eclectic psychotherapy combined with maternal psychoeducation etc.). The classification of interventions was based on their descriptions provided in the articles and did not consider any pre-defined inclusion criteria, such as the existence of previous evidence to support their potential effectiveness.

We used the risk of bias (RoB) tool 2.0 from the Cochrane Collaboration [22], which assesses six RoB dimensions: 1) bias arising from the

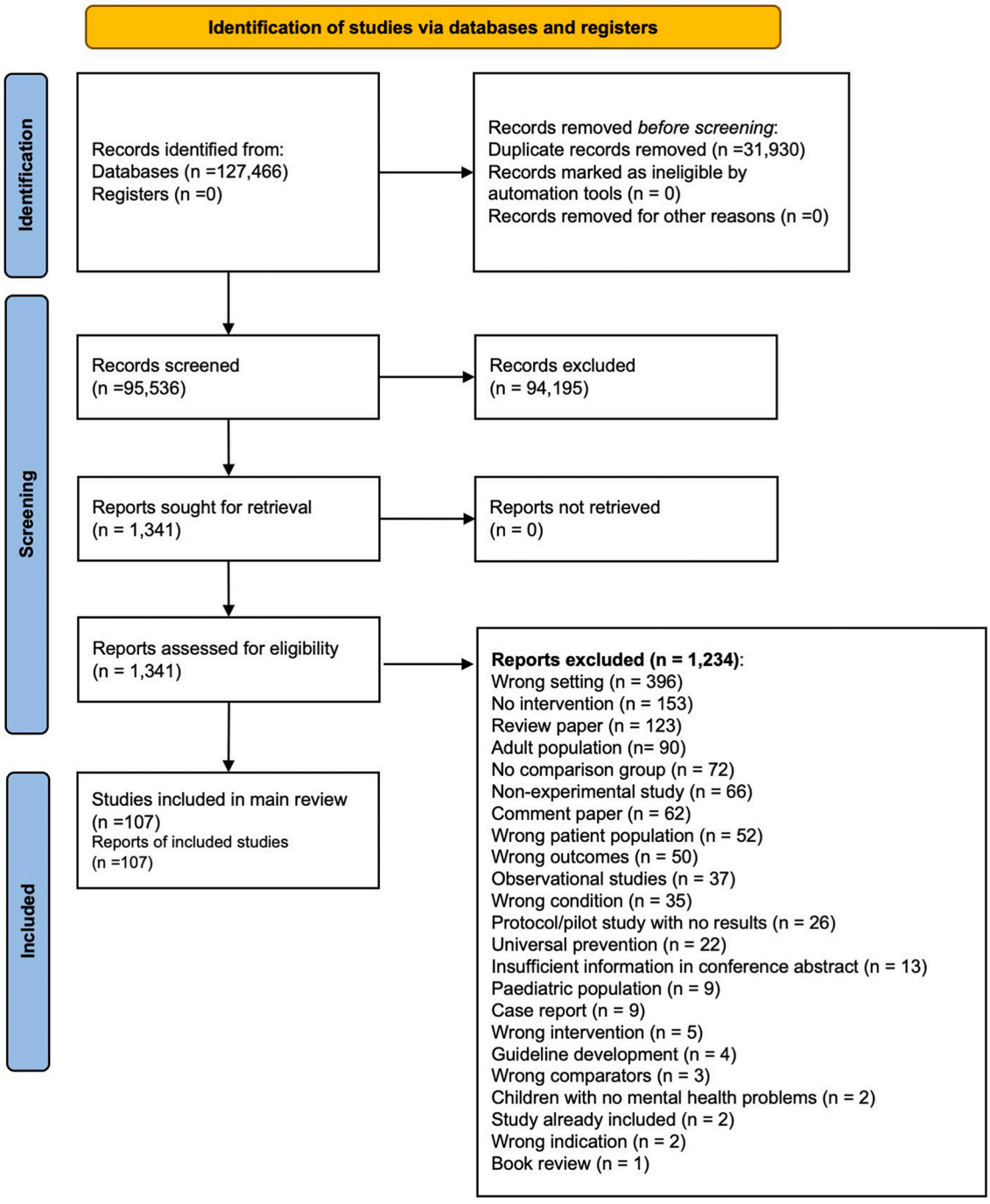

Fig. 1. PRISMA flowchart.

randomization process; 2) bias due to deviations from intended intervention; 3) bias due to missing outcome data; 4) bias in measurement of the outcome; 5) bias in selection of the reported result; and 6) overall risk of bias of included studies.

A formal ethical approval was not necessary because our study only used data published in the scientific literature and, therefore, did not involve contact with research participants.

2.3. Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

3. Results

127,466 records were identified through the database search. We did not identify any additional records through other sources. 31,930 were duplicates and were excluded. After screening titles and abstracts

94,195 were excluded, resulting in 1341 full texts being assessed for eligibility. From these, 1234 were excluded, resulting in a total of 107 studies being included in the narrative synthesis. Table 1 lists all studies included in the review and presents their key characteristics, and Fig. 1 shows the PRISMA flow chart of the screening and assessment process.

Studies were carried out in 26 different LMICs. Almost half of the studies came from Iran ($n = 52$; 48.6%) [10,23–71]. China [72–77] and India [78–83] contributed six (5.6%) studies each, and Brazil [84–88] five (4.8%), while Palestine [89–92], Sri Lanka [93–96] and Turkey [97–100] contributed four (3.8%) each. Seven other countries contributed two (1.9%) studies each [101–114], and twelve countries one (0.9%) each [115–126].

Over two-thirds of studies ($n = 85$; 79%) were randomised clinical trials (RCT) [23,27–36,39–41,43–46,48,49,51–53,56,58–83,85–88,90–92,94–97,99,100,102–105,108–114,116,117,119–123,125–128]. However, over a half of these RCT studies ($n = 47$; 55.3%) reported no procedures to guarantee blindness [27,29,31,36,41,44,45,49,51,56,64,66,70,72–75,79,80,82,86,87,90–92,94,96,97,99,100,102,103,108,111–114,117,119–121,123,126–128].

All 107 studies focused on interventions to treat mental health problems. Therefore, no studies on prevention were found. Included studies addressed 19 different conditions. ADHD ($n = 43$; 40.2%) [10,23,24,30,31,33–35,38,40,43,44,48,50–53,55–65,67,69,72,74,77–79,81,82,84,87,95,100,106,120], PTSD ($n = 21$; 19.6%) [46,73,90–94,96,104,107–110,113–115,118,119,121,122,126] and anxiety disorder ($n = 11$; 10.3%) [27,32,36,37,49,70,85,88,97,99,101] were the conditions with the highest number of studies. The primary outcome assessed by the majority of studies ($n = 94$; 87.8%) was the reduction of core psychiatric symptoms [10,23–25,27,28,30–52,54,56–74,76,78–83,85,87,88,90–105,107–110,112–122,124,126–128].

Eight different types of intervention were tested by the studies included in the review, with psychotherapy ($n = 45$; 42.1%) [26,27,29,36,37,43,46,47,49,56,70,71,73,76,84,86,90–94,96,98,99,101–105,108–114,117–119,121,122,124,126,127] being the most commonly evaluated, followed by pharmacological interventions ($n = 20$; 18.7%) [28,30,31,35,39,41,44,48,52,57,60–62,67–69,77,79,80,85].

Detailed distribution of studies according to key variables is provided as Supplemental Table S1 (Appendix 2).

The most common comparator was no intervention ($n = 43$; 40.2%) [10,25–27,29,36–38,42,46,51,53,56,66,69,73,75,89–93,96,97,100–103,105,107,110,112–114,116–119,121,124,126,128]. In over a quarter of studies ($n = 28$; 26.2%), participants in control groups received pharmacological interventions [28,30,31,34,35,41,44,45,48,52,55,60–62,64,69,71,72,77,79,80,84,86,98,99,120,122]. Other comparators included active control [24,49,59,74,76,81,83,87,88,94,104,108,111,123], placebo [43,78,85,95,125], or combined comparators (e.g., pharmacological interventions combined with placebo [23,33,39,40,58,63,65,125] or with active control [32,50]). A detailed description of types of comparators by types of intervention is provided in Supplemental Table 2 S2 (Appendix 2).

Some key features of interventions are presented in in Supplemental Table S3 (Appendix 2). The most common settings were schools ($n = 37$; 34.6%) [10,25,26,36,37,46,47,53,54,56,66,73–75,83,87,89,90,92,93,96,97,102,105,107–112,114,116,117,121,123,126,128] and outpatient clinics ($n = 35$; 32.7%) [23,24,27,28,30–33,35,39,40,42,48,49,55,58,60–63,67,69–71,77,79,80,84,86,88,95,98,99,118]. Over one-fifth of studies did not report the settings in which interventions were delivered [34,38,41,43,50,51,57,59,64,65,68,72,78,82,85,100,101,104,106,119,120,125,127].

Interventions were mostly delivered in one-to-one configuration ($n = 58$; 54.2%) [10,25,28–31,33–41,43–46,48,50–52,57–69,72,74,77–81,84,85,87,88,94,95,98,99,104,106,113,120,123,125,127] or in groups ($n = 34$; 31.5%) [24,25,42,49,53–56,70,71,73,75,76,83,86,89–92,96,97,100,102,105,107,109,111,112,114,116,121,124,126]. The most common types of practitioners reported as delivering the interventions were psychologists ($n = 21$; 19.6%) [26,46,47,53,55,56,71,73,76,87,91,101,103,105,108,111,113,115,127,128] or psychiatrists ($n = 13$; 12.2%) [10,27,30–33,39,51,66,67,69,70,117]. A variety of other delivery agents also delivered interventions, for example, other mental health professionals ($n = 6$; 5.6%) [36,42,49,86,88,124], teachers ($n = 9$; 8.4%) [89,90,93,94,98,106,112,116,118] and lay people (n = 9; 8.4%) [78,92,96,102,104,114,122,125,126]. Over one-third of studies ($n = 42$; 39.2%) did not report or did not specify by whom interventions were delivered [10,24,25,29,34,35,37,40,41,43–45,48,50,52,54,58,60,62–65,68,72,74,75,77,79,80,82–85,95,97,107,119–121,123].

As far as differences between interventions and comparators are concerned, in over half of the studies ($n = 60$; 56.1%) there were no differences between interventions and comparators [23,25,27,28,30–36,38–42,44,45,48,49,52–54,56,58–60,62,63,65–71,73,77,79–81,84,85,91,94,97–99,104–106,108,116,120,121,123,124,126]. In 37.4% of studies ($n = 40$), Interventions were more effective than comparators [10,24,25,29,37,43,46,47,51,57,64,72,75,76,78,82,83,86,87,89,90,92,93,95,100,102,107,109–114,117–119,122,125,127,128]. Among conditions with a minimum number of studies to provide meaningful statistics, depression ($n = 5$; 62.5%) [83,102,112,117,128] and PTSD ($n = 12$; 57.1%) [46,90,92,93,107,109,110,113,114,118,119,122] were the ones with the highest proportion of studies with positive results. Among the different types of interventions, the highest proportion of positive results were for psychoeducation ($n = 6$; 54.5%) [26,75,83,89,100,107] and psychotherapy ($n = 22$; 48.9%) [24,29,37,46,47,76,86,90,92,93,102,109–114,117–119,122,127] – whereas psychoeducation interventions with positive results included several different ones (e.g., emotional intelligence training, positive parenting programme), with a limited number of studies each, 54% ($n = 12$) of the 22 psychotherapies found to be effective were CBT interventions. This corresponds to almost 60% of all studies on CBT presenting positive results.

Types of interventions varied across conditions. The distribution of interventions by conditions, including their effects and RoB, is provided in Supplemental Table S4 (Appendix 2).

As far as risk of bias is concerned, nearly one-third of studies presented low RoB ($n = 35$; 32.7%) [23,30,31,33–35,40,41,48,52,60–63,65,67,69,74,76–78,86,88,94–96,100,102,103,109–111,122,125,127]. ADHD was the condition with the highest number of studies classified as low RoB ($n = 21$; 48.8%) [23,30,31,33–35,40,48,52,60–63,65,67,69,74,77,78,95,100]; anxiety ($n = 8$; 72.7%) [27,36,37,49,70,85,97,99] and PTSD ($n = 15$; 71.4%) [46,73,90–93,107,108,113–115,118,119,121,126] were the conditions with the highest number of studies classified as high RoB. Dietary supplementation ($n = 9$; 81.8%) [23,33,34,40,63,65,78,95,125] and pharmacological interventions ($n = 12$; 60.0%) [30,31,35,41,48,52,61,62,67,69,77] were the types of interventions with most studies being classified as low RoB. 66.7% (n = 8) of studies on neurocognitive interventions were classified as presenting some concerns [45,51,59,64,81,82,87,128], the main reason being due to studies not reporting any procedures to guarantee that outcome assessors were blind to participants' group assignment. For all other types of interventions, more than half of studies were classified as presenting high RoB. The main reasons for studies being classified as high RoB was due to lack of blindness in the assessment of outcomes and lack of randomization in participants' group allocation.

4. Discussion

In our systematic review, we mapped interventions for the treatment of mental health problems among young people in LMICs. We identified a substantial number of studies ($n = 107$) covering a range of child and adolescent mental health problems ($n = 19$) and different approaches ($n = 8$) to treat these problems. Although we searched for interventions

focused on prevention of mental health problems, we did not find any studies assessing such types of intervention. Our review help expand knowledge in the field by summarising the growing body of evidence on the treatment of child and adolescent mental health problems in LMICs – we found that, in less than one decade, the number of intervention studies in LMICs increased by nearly 60%, so there is now robust evidence on effective interventions that can be implemented in LMICs in different setting in the public health systems.

Our main results show that several interventions have been shown to be effective in treating youth mental health problems in LMICs, particularly psychoeducation and psychotherapy, with 54.5% and 48.9% of studies finding positive results respectively, as well as interventions to treat depressive disorders and PTSD, with 62.5% and 57.1%.

In comparison to a similar systematic review published in 2013 [8], the number of RCTs carried out in LMICs increased by almost 60% (from 54, up to August 2011[8] to 85 in our review). In addition to the increase in the number of RCTs, quality of studies seems to have slightly improved as well – while the quoted review [8] reported that "very few" trials included in their review met the expected "high standards", the proportion of studies classified as high RoB decreased from 55% among studies published until 2011 to 43.7% among those published after 2011. As a result, there is now a variety of interventions that have the potential for being implemented in LMICs, from those which require specialists and/or highly trained professionals to be delivered, such as psychotherapy, pharmacological and neurocognitive interventions, to less complex and potentially low-cost ones, such as psychoeducation, meditation, and dietary supplementation. Those interventions have been tested to treat some of the most common and impactful mental health problems among children and adolescents. Until recently, most of the robust evidence available came from HICs – e.g., Klasen et al. (2013) [8] found no RCT on treatment for depressive and anxiety disorder and only three studies on ADHD in LMICs, all of them focused on pharmacological interventions. In contrast, the authors reported robust evidence from HICs on the effectiveness of psychosocial interventions to treat such conditions, which may not be generalisable to LMICs due to socioeconomic and sociocultural differences between HIC and LMICs [8,12,129].

Among studies which reported who delivered the interventions, 1/3 of psychotherapies and of psychoeducational interventions were delivered by teachers or lay people, and 61% of all interventions delivered by these professionals were superior to comparators. Considering that specialised professionals are scarce in many LMICs [130], the fact that there are several interventions demonstrating effectiveness when delivered by non-specialised professionals and lay persons should increase potential for implementation in different contexts, particularly in settings with limited human resources.

It is noteworthy that, in our review, most studies on pharmacological interventions found no differences between interventions and comparators. In the majority of such studies (80%), an off-label medicine was compared to one that had already been proven effective – in this context, "off-label" refers to the use of any medication that is not listed in the medical guidelines or scientific literature to treat the medical condition to which it is being used, an example being buspirone, which is usually prescribed to treat anxiety disorders, being tested as an alternative to treat ADHD, as compared to methylphenidate, which is the first pharmacological choice to treat this condition [131]. None of these studies showed a difference between intervention and comparators, suggesting that the newer pharmacological treatment being evaluated had similar performance to the already well-established one. Some of the newer pharmacological alternatives which were tested, for example, modafinil, are likely expensive and difficult to access in many LMICs. However, other options such as buspirone or bupropion may be more available than the first line treatment Methylphenidate and this could be useful for increasing the number of pharmacological treatments which could be considered in settings where there are barriers in relation to supply/availability, or restrictions due to regulations or policy priorities. In Brazil, for example, which ranked 7th among the major importers of methylphenidate, this medication is no longer included in the Ministry of Health's list of essential medicines and doctors are required to fill a "controlled-drug form" to prescribe it. As a result, in many parts of the country the medication is not easily available in public health services [132].

It is also noteworthy that several non-pharmacological interventions were found to be effective, which confirms results reported in a recently published umbrella review [133].Considering that, among children and adolescents, non-pharmacological treatment should be prioritised over pharmacological ones [134], this review provides evidence to support policymakers and practitioners in identifying non-pharmacological interventions that could be implemented in different settings, particularly in community-based health services using the available resources. Our results suggest that some psychoeducation interventions, such as emotional intelligence training and positive parenting programme, and, that CBT, in particular, are the ones with most promising results and should, therefore, be prioritised in mental health policymaking in LMICs.

This systematic review has several strengths: Firstly, considering that our main goal was to map interventions focused on treatment and prevention of child and adolescent mental health problems in LMICs, we prioritised sensitivity over specificity in our search strategy, which resulted in a very comprehensive search that was able to identify studies covering the most important mental health problems that affect children and adolescents and a variety of interventions to deal with these conditions. It is very likely that, as a result of this search strategy, we were able to identify, if not all, at least the most relevant studies in this field, which may have provided us with a robust set of evidence on interventions that might be implementable in most LMICs. The references that were retrieved from the electronic databases went through a rigorous methodological process, by a team of well-trained researchers led by experts in the field. Therefore, the systematic review was executed following high-quality standards, which support the reliability of our results.

Notwithstanding, this review has some limitations that should be taken into consideration. From a methodological point of view, although we contacted corresponding authors at least twice, we failed to retrieve missing data and to clarify potential inconsistencies in many studies. We were not able, for example, to estimate SMD and 95% CI for 16 (14.9%) studies and, therefore, had to rely mostly on the authors' narratives to decide whether results were positive or not. Therefore, one should be cautious when considering such results. If on one hand our search strategy provided us with a comprehensive set of references, most certainly covering all the available evidence, it also resulted in a significant heterogeneity of studies, which limited our possibility to draw more extensive comparisons using, for example, meta-analytical approaches. Nonetheless, the comparisons we were able to make certainly provide important insights on potential opportunities for implementation of effective mental health care in LMICs.

Some important considerations also emerged from the final set of studies included in our review. First, there was an overrepresentation of some countries – particularly Iran, which contributed almost half of the available evidence. Additionally, notwithstanding the variety of countries (26 in total), most of these countries contributed a very limited number of studies. These results suggest that while some countries like Iran may now have strong scientific groups undertaking the challenge of advancing clinical research, most LMICs still lack human and economic resources to carry out studies that are needed to fill both the scientific and the care gaps in LMICs.

As a result, for most countries there is still limited evidence on which interventions work best in that particular setting. It may be that interventions tested in one LMIC would not be adequate for other similar countries. LMICs comprise a very heterogeneous group of countries which, albeit sharing similar levels of economic development, may yet differ substantially as far as sociocultural characteristics and political

Panel: Research in context

Evidence before this study

Since 2007, mental health of young people has been acknowledged as a major public health challenge worldwide, particularly in low- and middle-income countries (LMICs), where most young people live. Although the prevalence of mental health problems and associated burden are greater in LMICs, most of the evidence on intervention to treat these problems come from high-income countries (HICs) – a review published in 2007, for example, found that 87% of trials on treatment and prevention of mental disorders came from HIC, whereas another one on child and adolescent mental health interventions, published in 2013 [8], found 54 trials carried out in LMICs, but concluded that the most robust evidence still came from HICs. Considering remarkable contextual differences between HICs and LMICs, particularly in relation to availability, or scarcity, of resources, transferring evidence from the former to the latter is not straightforward. Therefore, an updated systematic review of trails carried out in LMICs would be very helpful to inform mental health policymaking in LMICs.

Added value of this study

Our systematic review provides a comprehensive synthesis of the available empirical evidence on interventions that have been tested in LMICs to treat mental health problems among children and adolescents. Our results show that several interventions have been proven effective in LMICs when delivered by specialist and non-specialist professionals, as well as by lay persons, in different settings, including several psychosocial interventions, which should be the first choice to treat mental health problems in this age group. Our results also show that, compared to finding of former reviews, the quality of the evidence has slightly improved. Nonetheless, the distribution of trials across LMICs remain remarkable unequal, with one single country contributing almost half of the studies, whereas most of the 26 countries represented in the review contributed a limited number of studies. Whereas our review shows that there are, now, several interventions that have the potential to be effectively implemented in LMICs, it also identified important limitations that need to be addressed to improve LMICs ability to close the mental health care gap among children and adolescents living in low-resourced settings.

Implication of all the available evidence

The main implication of the available evidence is the fact that several interventions have been tested and proven effective in LMICs. Considering that transferring evidence from HICs to LMICs is not straightforward due to contextual and socioeconomic features, evidence from LMICs is very important to inform the implementation of interventions in countries which share similar contextual characteristics. Nonetheless, considering that LMICs comprise a very heterogeneous group of countries, interventions that have been tested in one country may need to be adapted to be implementable in other countries.

By highlighting the overrepresentation of some countries and underrepresentation of others, our review helps to identify persisting research gaps which should be considered in future research initiatives, particularly those related to global mental health research, which should invest efforts in research capacity building in countries where evidence is very limited or inexistent.

The fact that several interventions have now been tested in LMICs provides policymakers and practitioners with evidence that might help them find interventions that can be implemented in their local health systems.

atmosphere, as well as types of deliverers available, are concerned. Therefore, transferring evidence from one LMIC to another may not be straightforward, although the WHO and other bodies recommend packages of interventions for LMICs even though evidence from these countries is limited [134].

It is noteworthy that almost 60% of studies were classified as presenting high risk of bias, whereas approximately one third were classified as low RoB. The high proportion of studies presenting some concerns and high RoB may mostly be attributed to studies testing non-pharmacological interventions, such as psychotherapy and psychoeducation. Considering the characteristics of such interventions, some of the features that comprise high-quality clinical trials, such as double-blindness and active comparators, may not be achievable. This perhaps helps explain why the majority of studies on non-pharmacological interventions provided participants in comparison groups with no interventions whatsoever. Such limitation seems to be common even in clinical trials on psychosocial interventions carried out in HIC, as some systematic reviews have shown [135–137]. One alternative to overcome such limitation in future studies would be to provide participants in control groups with some sort of mock/sham intervention. This, however, might have important ethical implications, in addition to increasing costs and complexity, making even more difficult for most LMICs to conduct high-quality clinical trials.

5. Conclusion

This systematic review provides a comprehensive set of evidence on interventions that have been proven effective for the treatment of child and adolescent mental health problems in LMICs. Whereas closing the mental health care gap remains a large and ongoing challenge in LMICs, there is evidence for a range of interventions which could be effectively delivered by different professionals in LMICs. We expect that our synthesis can be used by policymakers and practitioners to identify effective interventions that can be implemented in different public health settings to support the mental health of young people in LMICs – for example, where specialist professionals are scarce, policymakers would be able to identify, in our review, interventions that have been proven effective when delivered by non-specialists which they could adopt as part of their mental health policy. We also expect that, from our review, researchers in LMICs can learn lessons that might help them improve the quality of further studies by, e.g., adopting strategies to reduce risk of bias, such as using active comparators and improving blindness. One important recommendation is that clinical trials conducted in LMICs should clearly report statistics parameters that might be comparable across different studies – preferably means and standard deviations. This would make possible for future systematic reviews to perform quantitative syntheses (meta-analysis) of the existing evidence, which are usually stronger than narrative syntheses.

It is important to note that these interventions may need to be adapted to be implemented in different sociocultural contexts, especially in settings with limited human resources. Such adaptation efforts might be worthwhile, as adapting existing interventions that have already been evaluated in low-resource settings can be more efficient than developing new interventions. Further research should test versions of these interventions that are tailored to different contexts to verify which adaptations work best to guarantee effectiveness in real-world contexts. Additionally, new research is needed on the development of implementation strategies that lead to the uptake and scaling-up of effective interventions across different LMICs, considering specificities of each country. Therefore, it is imperative that academics develop knowledge translation strategies and tools together with practitioners to implement collaborative approaches for sharing this evidence among relevant

stakeholders in LMICs, so it can be translated into policymaking and into the implementation of adequate effective interventions to increase young people's access to effective mental health care.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.comppsych.2022.152358.

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